REMARKS

Applicants have received and reviewed the Final Office Action dated April 20, 2004. Applicants request entry of the Amendment and withdrawal of the rejection and objections of the claims.

Claims 1, 27-41 and 43-73 are pending in the application. Claims 1, 27-38, 44-56 and 59-71 are rejected. Claims 39, 40, 57, 58, 72 and 73 are objected to. Claims 41 and 43 are allowed.

Claims 39, 40, 57, and 58 were objected to as being dependent upon a rejected base claim. These claims are written in independent form, and consequently are allowable. Withdrawal of the objection to claims 39, 40, 57, and 58 is respectfully requested.

Claims 1, 39-40, 44, 57, and 58 are amended. Support for the amendments can be found in the originally filed claims and throughout the specification including at page 5, line 24 to page 6, line 2.

Claims 27, 29-33, 42, 45, 47-51, and 59-73 are canceled without prejudice. Applicants reserve the right to pursue the subject matter of these claims in continuing applications.

New claims 74-76 are presented. The new claims are supported throughout the specification and originally filed claims. Applicants submit the newly presented claims do not raise any issues of new matter.

Written Description

The Examiner rejected claims 1, 27-38, 44-56, and 59-71 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Applicants have canceled claims 27, 29-33, 45, 47-51, and 59-71 rendering the rejection of these claims moot. Applicants respectfully traverse this rejection with respect to the other claims.

The Examiner alleges the specification provides insufficient written description to support the genus encompassed by the claims. Applicants' claims, as amended, are directed to methods of screening comprising analyzing expression of a polypeptide having at least 95% sequence identity to SEQ ID NO:1 or 2 wherein the polypeptide has uncoupling activity.

The written description requirement is satisfied when Applicants' specification conveys with reasonable clarity to those skilled in the art, that as of the filing date sought, he or she was in possession of the invention. *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); *Vas-Cath Inc. v. Mahurkar,* 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). A written description of an invention involving a chemical genus requires a precise definition, such as by structure, formula ... of the claimed subject matter sufficient to distinguish it from other materials. *Univ. of California v. Eli Lilly and Co.,* 43 USPQ2d 1398. 1405 (Fed. Cir. 1997) (emphasis added). Since one skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass, such a formula is normally an adequate description of the claimed invention. *Id.* at 1406 (emphasis added).

The written description is presumed to adequately support the claims until the examiner presents sufficient evidence to rebut the presumption. See, e.g. See, e.g., *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). The examiner must have a reasonable basis and has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. In re Wertheim, 191 USPQ 90, 97 (CCPA 1976). A general allegation of "unpredictability in the art" is not a sufficient reason to support a rejection for lack of adequate written description. MPEP 8th Ed., Rev.2, §2163 IIIA.

The Examiner's rejection of claims 1, 27-38, 44-56, and 59-71 is primarily based on the assertion that applicants have not identified variants, nor polypeptides that are at least 95% identical to human OGC, which possess the ability to change mitochondrial membrane potential. Applicant's respectfully disagree and assert that human OGC variants that having at least 95% sequence identity and uncoupling activity are readily appreciated by one of skill in the art based on the specification and knowledge in the art. Furthermore, the Examiner fails to present sufficient evidence that one of skill in the art could not appreciate OGC variants having at least 95% sequence identity, and that possess uncoupling activity.

At the time of filing, human OGC (2-oxoglutarate carrier protein) and naturally occurring variants were known in the art. However, at that time, it was not known that human OGC had uncoupling activity. The present invention is related to the discovery that human OGC,

including native homologues and variants (page 26, lines 1-4), has uncoupling activity. In support of their discovery, the inventors demonstrated that human OGC comprising a sequence of SEQ ID NO:2 has uncoupling activity. Knowledge in the art indicates variants of human OGC have a high degree of conservation, especially in three identified functional domains. This is supported by the two disclosed native variants of human OGC, which have 99% sequence identity to each other. (See the specification at page 5, lines 20-23) A NCBI BLAST search of an amino acid sequence of the polypeptide encoded by SEQ ID NO:2 (GenBank Accession No. AF070548) revealed 95% or greater sequence identity with the known variants of human OGC, as well as other mammalian OGC proteins. (Exhibit A) Additionally, the bulk of variation occurs outside of the three known functional domains. (Exhibit B)

Moreover, the specification directs one of skill in the art to align the OGC sequences to homologous sequences and minimize the number of amino acid changes made in regions of high homology. (See the specification at page 27, lines 18-22) Using the sequences provided in the specification, Applicants submit one of skill in the art could readily envision polypeptides that have at least 95% sequence identity to a polypeptide that is encoded by SEQ ID NO:1 or SEQ ID NO:2.

The Examiner also asserts that because there is insufficient written description, one of skill in the art would not know how to make or use the claimed method without performing additional experimentation. Applicants request clarification of the rejection as the Examiner's comment's seem more properly directed to an assertion of lack of enablement, for which a formal rejection, including the required *prima facie* showing, has not been made. Under enablement standards, an applicant's specification must enable a person skilled in the art to make and use the claimed invention without undue experimentation. The fact that experimentation is complex, however, will not make it undue if a person of skill in the art typically engages in such complex experimentation.

Applicants' object to the Examiner's statements and assert that undue experimentation is not required. Given the knowledge of OGC in the art, including the degree of conservation between variants and well known functional domains, one of skill in the art can readily appreciate the chemical structure (i.e. sequences) of OGC variants and test to confirm the uncoupling activity, if desired. Applicants submit that such testing is not undue experimentation.

Summary

With entry of this Amendment, claims 1, 28, 34-38, 44, 46, and 52-56 are in condition for allowance and claims 39-41, 43, 57, and 58 are allowed or allowable. Applicants respectfully request a Notice of Allowance. Applicants believe the Examiner's rejections and objections have been addressed, but if any issues remain, the Examiner is invited to telephone the undersigned at the below listed telephone number.

Respectfully submitted,

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Date

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